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3D/4D Printing Hydrogel Composites: A Pathway to Functional Devices

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ABSTRACT

The past few years have seen the introduction of a number of 3D and 4D printing techniques used to process tough hydrogel materials. The use of 'color' 3D printing technology where multiple inks are used in the one print allows for the production of composite materials and structures that can further enhance the mechanical performance of the printed hydrogel. This article reviews a number of 3D and 4D printing techniques for fabricating functional hydrogel based devices.

INTRODUCTION

3D printing is an additive manufacturing technology that has been used to process hydrogel materials for tissue engineering applications. A major limitation in the use of hydrogels has been their poor mechanical performance but the last two decades has seen the development of a range of 'tough' hydrogels. [1] These developments have been followed by the introduction of new printing techniques that can form tough hydrogels into complex structures. [2,3] The mechanical properties of these printed tough hydrogels tend to be inferior to those prepared using casting under optimal lab conditions. Table I compares the mechanical parameters of alginate (Alg) / poly(acrylamide) (PAAm) ionic covalent entanglement (ICE) gels when cast and printed.

Table I. Summary of the mechanical properties of cast Alg/PAAm ICE gels (data reproduced from ref. [4]) and printed Alg/PAAm ICE gels (data reproduced from ref. [2]).[a]

	E [kPa]	σ_T [kPa]	ε_f [%]	U [MJ/m^3]	Q
Cast	29	156	2300	~2.5	7.1
Printed	66 ± 5	170 ± 30	300 ± 20	0.26 ± 0.01	6.7

[a] E is the elastic modulus, σ_T is the tensile strength, ε_f is the failure strain, U is the work of extension and Q is the swelling ratio.

The formation of composite materials is an established means of enhancing the mechanical properties of constituent materials. 'Color' or multi-material 3D printers can print stronger reinforcing materials alongside tough hydrogel inks to form composites. In this article we demonstrate how 3D printing techniques can be adapted to fabricate functional hydrogel based devices.

EXPERIMENT

Materials

All materials were used as-received and all solutions were prepared using Milli-Q water (resistivity = 18.2 Ω cm). α-Keto glutaric acid photo-initiator was purchased from Fluka (Australia). Acrylamide (AAm) solution (40%, for electrophoresis, sterile-filtered), alganic acid sodium salt (from brown algae with Brookfield viscosity 2% in H_2O at 25 °C of 250 mPa s), calcium chloride (minimum 93.0% granular anhydrous), ethylene glycol (rheology modifier), N-isopropylacrylamide (NIPAAm) and N,N'-methylenebisacrylamide (MBAAm) crosslinker were purchased from Sigma Aldrich (Australia). A commercial epoxy based UV-curable adhesive Emax 904 Gel-SC (Emax) was purchased from Ellsworth Adhesives (Australia).

Hydrogel Ink Formulations

An alginate ink for printing dissolvable support structures was prepared by mixing 3.75 ml of ethylene glycol in 11.25 ml of a 0.1 M calcium chloride stock solution. A spatula was then used to dissolve 450 mg of alganic sodium salt into the printing solution.

An Alg/PAAm ICE gel ink was prepared by dissolving 4.50 ml of AAm, 38.7 mg of MBAAm, 36.9 mg of α-keto glutaric acid and 3.75 ml of ethylene glycol in 6.75 ml of a 0.01 M calcium chloride stock solution. The ethylene glycol was used as a non-volatile co-solvent with the volume ratio of ethylene glycol to water fixed at 1:2.5. A spatula was then used to dissolve 450 mg of alganic sodium salt into the printing solution.

An Alg/NIPAAm ICE gel ink was prepared by dissolving 3 g of NIPAAm, 15 mg of N,N'-methylenebisacrylamide and 90 mg of α-keto glutaric acid in 15 ml of a 0.01 M calcium chloride stock solution. A spatula was then used to dissolve 450 mg of alganic sodium salt into the printing solution.

3D Printing

Fibre reinforced hydrogels, adhesion test samples and a smart valve were all fabricated with an EnvisionTEC 3D-Bioplotter system that was coupled with a commercial UV-curing system. The patterned inks were cured with a Dymax BlueWave 75 Rev 2.0 UV Light Curing Spot Lamp System using a 19+ W/cm^2 UV source with a 1 meter light guide. Digital models of tensile specimens and the multi-component valve were prepared with computer-aided design (CAD) software (Solidworks). The composite materials were designed by creating an assembly of separate parts. EnvisionTEC software was used to slice the digital models into a stack of two dimensional layers (250 μm thick) to determine the print path. Material files and internal structures were then added to each part within the assembly.

The extrusion inks were loaded into the 3D-Bioplotter in separate pressurized syringe barrels which were positioned into the temperature controlled print heads. Each barrel was fitted with a 23 gauge syringe tip (diameter 0.337 mm) and maintained at stable temperature of (25 °C for the Alg/PAAm ICE gel and Emax inks and 10 °C for Alg/NIPAAm ICE gel ink) during printing. A pressure between 0.5 and 1 bar was used to extrude the inks and a head speed between 5 and 20 mm/s was used to pattern them. The inks were pinted with a 0.5 mm resolution

onto a poly(pyropylene) sheet when printing with the Alg/PAAm ICE gel ink or a glass sheet cooled to 10 °C when printing the Alg/NIPAAm ICE gel ink. The UV light was passed over each layer of patterned ink for 50 s and 200 s for the final layer. A spatula was used to remove any of the alginate based ink for printing sacrificial support structures once the print was finished. Finally the printed ICE hydrogels were immersed in 0.1M calcium chloride (72 hr) to fully crosslink the alginate.

Particulate reinforced hydrogels and gradient structures were fabricated with a custom built 3D printer. The 3D printer was built around a Sherline 8020 CNC milling stage and a novel syringe controlled deposition system made up of two Zaber T-LA60A-KT03 Miniature Linear Actuators mounted to the CNC gantry. Plastic tubing and a Y-adaptor was used to direct the flow from two syringes into a single stream. A disposable static chaotic mixer with 12 mixing elements (Nordson EFD) was added below the Y-adaptor to insure blending of the two streams. A custom 3D-printed nozzle was designed to extrude a flat ribbon of material having a rectangular shaped outlet with dimensions 1.5 mm by 15 mm. An Opsytec Dr. Gröble 365 nm UV-LED smart light source was attached near the deposition system so that its illuminated area followed the print head to cure dispensed ink.

The extrusion inks were loaded into the 3D printer in separate syringe barrels. The Emax volume fraction was controlled using custom software (developed in C#, using Visual Studio 12.0) that allowed the two inks to be dispensed in different ratios by adjusting the speed of the two linear actuators. The net flow rate of combined material out of the nozzle had to remain constant to maintain consistency; thus the individual flow rates of the two materials from each barrel were adjusted relative to each other throughout the print. For gradient printing the flow rate of the two materials had to be linearly ramped; the speed of depression in one barrel was decreased from 100% to 0% while simultaneously the other barrel experienced a speed increase from 0% to 100%. The combined total rate of extension of the two linear actuators was set at a constant 180 μm/s when the milling stage was moved with a speed of 80 mm/min. The UV light using 100 % intensity followed the extrusion nozzle to set the blended composite structure by partially curing the two inks.

A processing scheme was applied to the composite ribbons after printing to improve their mechanical properties. The Dymax BlueWave 75 Rev 2.0 UV Light Curing Spot Lamp System using a 19+ W/cm^2 UV source with a 1 meter light guide was used to complete the curing process. Each 30 mm length of ribbon was exposed to the spot of UV irradiation for 30 s. The composites were then immersed in 0.1 M aqueous calcium chloride solution for 72 hr to fully crosslink the alginate polymer network.

Adhesion Testing

An adhesion test was performed on a Shimadzu EZ-L Universal Mechanical Tester. An adhesion test sample was printed with Emax ends and a band of the Alg/PAAm ICE gel. The adhesion sample was extended at a rate of 10 mm/min in the direction perpendicular to the Alg/PAAm ICE gel band until failure and the position of failure was noted. Four repeat tests were performed on each material with errors estimated from one standard deviation.

DISCUSSION

Emax 904 Gel-SC is a commercially available epoxy based UV-curable adhesive that has been identified as a suitable ink for printing composite structures with the Alg/PAAm ICE gel ink. These two inks can be incorporated into the one printing process because they have similar rheological properties, are both cured by UV initiated free radical polymerization reaction and display strong adhesion. [5] Adhesion between materials is important when forming composites for transferring stresses from the matrix onto the reinforcing phase. Adhesion is also important when fabricating multi-component devices as interfaces can act as a point of weakness in the devices structure. Figure 1a. shows a 3D printed Alg/PAAm ICE gel and Emax adhesion test sample clamped to a universal mechanical tester. Figure 1b. shows that the strained sample fails through the hydrogel band and not at the interface of the two materials. This demonstrates a strong adhesion between the Alg/PAAm ICE gel and Emax when the two inks are cured simultaneously side by side.

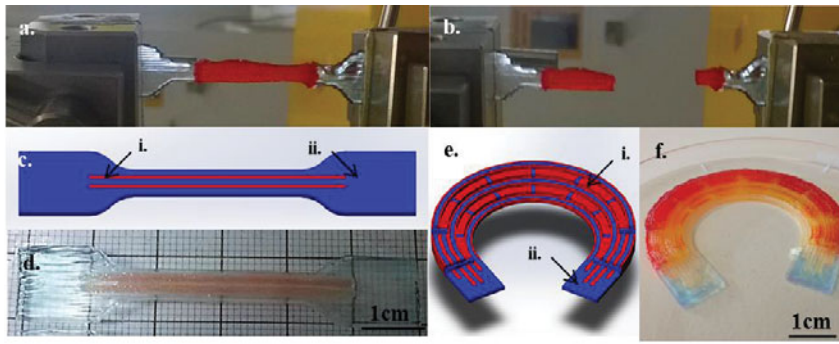

Figure 1 Photographs of Alg/PAAm ICE gel and Emax adhesion test sample (a.) before and (b.) after mechanical failure. (c.) CAD model and (d.) photograph of 3D printed fibre reinforced Alg/PAAm ICE gel composite tensile specimen. Labels indicate components to be printed with (i.) Alg/PAAm ICE hydrogel ink and (ii.) Emax. (e.) CAD model and (f.) photograph of 3D printed fibre reinforced Alg/PAAm ICE gel composite artificial meniscus. Images were adapted with permission from (Ref. [5]). Copyright (2014) American Chemical Society.

Fibre reinforced hydrogels have been made with a method that uses digital modelling and a 'colour' 3D printer to pattern two inks within the one structure. The models are made up of an assembly of two parts, one for the matrix and one for the fibre reinforcement. Fibres are designed as long thin volumes of material. When printing the models a different ink is assigned to each part of the assembly. Figure 1c. is an example CAD model of a fibre reinforced tensile specimen and Figure 1d. is a photograph of the tensile specimen printed with the Alg/PAAm ICE gel and Emax inks. The volume fractions of the printed materials can be altered by changing the number of fibers included in the CAD model. Tensile testing of the printed materials has shown that composites with higher volume fractions of Emax fibers display greater tensile strength and modulus. [5] The versatility of digital modeling enables these composites to be fabricated directly into complex shapes and useful structures. Figure 1e. is a CAD model of an artificial meniscus and Figure 1f. is a photograph of the artificial meniscus printed with the Alg/PAAm ICE gel and Emax inks.

A novel extrusion based deposition system was used to print particulate reinforced hydrogels. The deposition system was designed with two digitally controlled syringe pumps that pushed the ink from two syringe barrels though a Y-adaptor into a single stream which flowed through a static mixer. The mixer ensured blending of the two inks before they were pushed out the extrusion nozzle. The Alg/PAAm ICE gel and Emax inks are immiscible and phase separate when mixed together and so UV light was attached to the 3D printer so that the blended inks could be cured as soon as they were extruded to limit the phase separation. Figure 2a. is a macrosope image that shows the two phase structure of one these printed materials. Changing the extrusion rates of the two syringe pumps allowed for composites to be printed with various volume fractions of Emax. Mechanical characterisation showed that composites with low volume fractions of Emax (<50 %) behave like particulate reinforced composites. Custom software allowed for the extrusion rates of the two pumps to be ramped during the printing process to create gradients of material composition across the extruded ribbon. Figure 2b. is a photograph of an artificial tendon containing two composition gradients that form a transition of modulus from one end to the other. [6] Figure 2c. is a picture of the artificial tendon attached to a skeleton.

Figure 2 (a.) Macroscope image of a 3D printed particulate reinforced Alg/PAAm ICE gel composite ribbon with an Emax volume fraction of 40 %. (b.) Photograph of an artificial tendon printed with Alg/PAAm ICE gel and Emax gradient structures. (c.) Photograph of a 3D printed artificial tendon attached to a skeleton.

More functional hydrogel based devices can be fabricated with a 4D printing process that combines the digital modelling process used to print fibre reinforced hydrogels with a stimuli responsive hydrogel ink. 4D printing is an emerging technology for creating structures that change their shape on-demand over time. A stimuli responsive tough hydrogel ink was made by replacing the PAAm component of the Alg/PAAm ICE gel ink with PNIPAAm. PNIPAAm is a thermally sensitive hydrogel that exhibits reversible volume transition at a critical temperature (~ 32-35 °C). Digital modelling allows for the design of structures that can harness this volume change in the same way that the skeleton harnesses the volume change of muscles to create movement. A smart valve that can open and close as a response to the temperature of the water flowing through the valve was printed to demonstrate the utility of this technique. [7] Figure 3a. is a CAD model of the smart valve. Figure 3b. is a photograph of the open smart valve after it had been exposed to a flow of 20 °C water and Figure 3c. is a photograph of the closed smart valve after it had been exposed to a flow of 60 °C water.

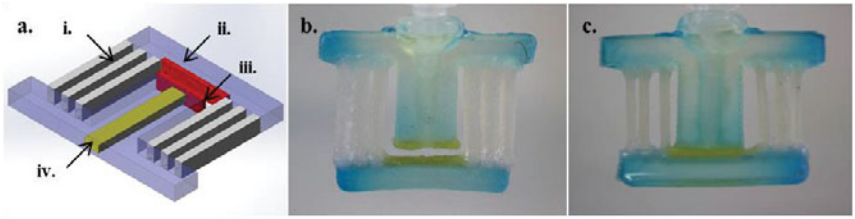

Figure 3 (a.) CAD model of hydrogel valve. Labels indicate components to be printed with (i.) Alg/PNIPAAm ICE hydrogel ink, (ii.) Emax, (iii.) Alg/PAAm ICE hydrogel ink and (iv.) the alginate based ink for printing sacrificial support structures. Photographs of the 4D printed valve open (a.) when swollen in water at 20 °C and (c.) closed when swollen in water at 60 °C.

CONCLUSIONS

We have introduced a number of 3D extrusion printing techniques used to make Alg/PAAm ICE gel and Emax composite materials. The customization of 3D printers and writing of new software were important steps in the development of the new printing techniques. The different techniques allow for the formation of composites with multiple reinforcement morphologies. The development of these 'color' 3D and 4D printing techniques has provided a pathway to fabricate functional hydrogel based devices demonstrated by production of an artificial meniscus, artificial tendon and a smart valve.

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